Remarks

Claims 27, 29, and 30 were pending in the subject application. By this Amendment, the applicants have amended claim 27. Support for the amendment to claim 27 can be found throughout the specification including, for example, at page 4, lines 8-12. No new matter has been added by the amendment. Accordingly, claims 27, 29 and 30 are before the Examiner for consideration.

The amendment to the claims has been made in an effort to lend greater clarity to the claimed subject matter and to expedite prosecution. The amendment should not be taken to indicate the applicants' agreement with, or acquiescence to, the rejections of record. Favorable consideration of the claims now presented, in view of the remarks and amendment set forth herein, is earnestly solicited.

Claims 27, 29, and 30 have been rejected under 35 U.S.C. §112, second paragraph, as being indefinite. The applicants respectfully traverse this ground for rejection to the extent that it might be applied to the claims as amended herein.

Claim 27 has been amended herein to clarify that capture reagents are homologs and/or orthologs of each other. The test for definiteness under 35 U.S.C. §112, second paragraph, is whether "those skilled in the art would understand what is claimed when the claim is read in light of the specification." *Orthokinetics, Inc. v. Safety Travel Chairs, Inc.*, 806 F.2d 1565, 1576, 1 USPQ2d 1081, 1088 (Fed. Cir. 1986). The applicants respectfully submit that the level of skill in the relevant art (molecular biology) at the time the subject application was filed was high. The terms "homolog" and "ortholog" are well-understood by the skilled artisan. Further, the skilled artisan would readily understand and be able to identify the capture reagents recited in the claims, especially in light of the specification at page 4, lines 10-12. Thus, the skilled artisan would have had no difficulty ascertaining the metes and bounds of the claims in light of the specification. Accordingly, reconsideration and withdrawal of this rejection under 35 USC §112, second paragraph, is respectfully requested.

Claims 27, 29, and 30 have been rejected under 35 U.S.C. §102(b) as being anticipated by Hoffman *et al.* (U.S. Patent No. 5,599,543). The applicants respectfully traverse this ground for rejection because the Hoffman *et al.* reference does not disclose each and every step of the

applicants' advantageous multi-analyte assay wherein a negative control is generated using the assayed sample.

It is basic premise of patent law that, in order to anticipate, a single prior art reference must disclose within its four corners, each and every element of the claimed invention. In *Lindemann v. American Hoist and Derrick Co.*, 221 USPQ 481 (Fed. Cir. 1984), the court stated:

> Anticipation requires the presence in a single prior art reference, disclosure of each and every element of the claimed invention, arranged as in the claim. *Connell v. Sears Roebuck and Co.*, 722 F.2d 1542, 220 USPQ 193 (Fed. Cir. 1983); *SSIH Equip. S.A. v. USITC*, 718 F.2d 365, 216 USPQ 678 (Fed. Cir. 1983). In deciding the issue of anticipation, the [examiner] must identify the elements of the claims, determine their meaning in light of the specification and prosecution history, and identify corresponding elements disclosed in the allegedly anticipating reference. *SSIH, supra*; *Kalman fv. Kimberly-Clarke*, 713 F.2d 760, 218 USPQ 781 (Fed. Cir. 1983)] (emphasis added). 221 USPQ at 485.

It is unclear how the "peptide circumsporozite protein regions of different parasite regions" cited by the Office Action would be considered negative controls (see page 3 of the Office Action). Hoffman *et al.* used as negative controls samples obtained from several assorted individuals ***different*** from those samples being assayed. See, col. 7, lines 40-45 and lines 57-59 and Table 3. For example, "negative serum controls" were persons with no history of exposure to malaria or "naïve" persons whereas the samples that were tested (assayed) were for individuals exposed to malaria (see "Study Population" in col. 6, lines 53-63). Unfortunately, as taught by the subject application, "[p]roblems may arise due to the fact that the source of the negative samples is different from that of the unknown sample [being assayed], resulting in unexpected reactivity." See, p. 2, line 29 through p. 3, line 2. Thus, Hoffman *et al.* teach negative controls that are quintessential examples of the problem being addressed by the applicants' claimed invention.

Contrary to the Hoffman *et al.* negative controls, the subject application recites claims in which a negative control is determined by measuring the reactivity of a sample toward capture reagents in an assay and identifying the least reactive capture reagent to the ***same*** sample as the negative control. In fact, the subject specification emphasizes that it is advantageous to select a negative control from the results obtained ***only with the same sample biological material being***

assayed because it obviates the step of processing a separate negative control material and addresses any problems that may arise related to unexpected reactivity to unrelated samples used as negative controls. See, p. 3, lines 1-2, 11-13 and 25-28.

Hoffman *et al.* do not disclose or suggest an assay wherein a negative control is generated via assessment of binding reactions to capture reagents within the ***same*** sample (sera) that is being assayed. Therefore, the applicants respectfully request reconsideration and withdrawal of the rejection under 35 U.S.C. §102(b) based on the Hoffman *et al.* reference.

Claims 27, 29, and 30 have been rejected under 35 U.S.C. §102(b) as being anticipated by Geyson *et al.* (Proc. Natl. Acad. Sci. USA 81:3998, 1984). The applicants respectfully traverse this ground for rejection because the Geyson *et al.* reference does not disclose each and every step of the claimed assay wherein a negative control value is derived from identifying the ***least*** reactive capture reagent to a sample being assayed.

As discussed above, the present invention requires the negative control be the least reactive capture reagent used in an assay for a given sample. The Office Action is of the opinion that the structurally similar peptides of Geyson *et al.* served as negative controls for the study (see page 3 of the Office Action dated October 28, 2008 and page 4 of the Office Action dated February 5, 2008). The applicants respectfully disagree with the Office Action's assessment. Geysen *et al.* teach the use of enzyme-linked immunoassays (ELISA) in identifying an immunogenic epitope of an important protein of foot-and-mouth disease virus. Specifically, various synthesized peptides were assayed using different antigens associated with the virus (see Figures 2 and 3 and Table 1). None of the assays performed with the different antigens were used in identifying a negative control; in fact, all of the binding reactions of the antigens to the samples were used to identify important analytes of the sample of interest. For example, scans 1-5 (as described in the article at pp.3999-4000) were all used in identifying the most reactive peptides as a possible epitope of the protein, whereas scan 6 served as a control for the assay.

In fact, Geyson *et al.* used the normal or average binding reactions, as opposed to the ***least*** binding reaction, of the peptides being tested in their sample as negative controls in their test (p.4000, section 3 of the Discussion, "***Except*** for cases in which either all or ***none*** of the peptides react, a large number of the peptides would effectively act as negative controls in the

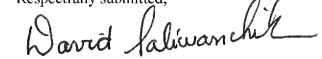
test. With adjacent peptides sharing a common sequence of five amino acids, the observation of peaks ***above a generally uniform background level*** would indicate a valid test." Emphasis added). Thus, in view of the remarks above, it cannot be said that Geyson *et al.* disclose each and every limitation of the claimed invention. The applicants' use of the least reactive capture reagent of an assay as a negative control differentiates the invention from the ELISA methods disclosed by Geysen *et al.* and others. Therefore, the applicants respectfully request reconsideration and withdrawal of the rejection under 35 U.S.C. §102(b) based on the Geysen *et al.* reference.

In view of the foregoing remarks and the amendment above, the applicants believe that the currently pending claims are in condition for allowance, and such action is respectfully requested.

The Commissioner is hereby authorized to charge any fees under 37 CFR §§1.16 or 1.17 as required by this paper to Deposit Account No. 19-0065.

The applicants also invite the Examiner to call the undersigned if clarification is needed on any of this response, or if the Examiner believes a telephone interview would expedite the prosecution of the subject application to completion.

Respectfully submitted,



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